

PATENT COOPERATION TREATY

IPD

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

To:  
**WOLF, GREENFIELD & SACKS, P.C.**  
 Attn. Finch, Stephen R.  
 600 Atlantic Avenue  
 Boston, MA 02210  
 UNITED STATES OF AMERICA

**DOCKETED**

**MAY 18 2005**

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT AND  
 THE WRITTEN OPINION OF THE INTERNATIONAL  
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

	Initials			
Confirmation		<input type="checkbox"/>	Date of mailing (day/month/year)	12/05/2005
Applicant's or agent's file reference	Docketing reference		6-12-05	
L0619.70003.WO				
International application No.	7-12-05 (2)		International filing date (day/month/year)	
PCT/US2004/043950	8-12-05		29/12/2004	
Applicant	mxn 222			
THE BRIGHAM AND WOMEN'S HOSPITAL, INC.				

1.  The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
 1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority  
 European Patent Office, P.B. 5818 Patentlaan 2  
 NL-2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

**Josef Ullrich**

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?** Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How?** Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**The amendments must be made in the language in which the International application is to be published.**

#### What documents must/may accompany the amendments?

**Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.**

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference  L0619 . 70003	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No.  PCT/US2004/043950	International filing date ( <i>day/month/year</i> )  29/12/2004	(Earliest) Priority Date ( <i>day/month/year</i> )  30/12/2003
Applicant  THE BRIGHAM AND WOMEN'S HOSPITAL, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b.  With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2.  Certain claims were found unsearchable (See Box II).

3.  Unity of invention is lacking (see Box III).

### 4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

THIOPHENE DERIVATIVES FOR UP-REGULATING HLA-DM ACTIVITY

### 5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

### 6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b.  none of the figures is to be published with the abstract.

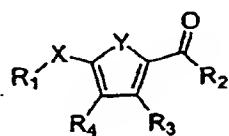
**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US2004/043950

**Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)**

Compounds of formula I, compositions, methods and kits are provided. The compounds and compositions may be particularly useful for modulating immunological responses.



I

wherein,

R<sub>1</sub> is alkyl, aryl, or heterocyclyl;R<sub>2</sub> is H, alkyl, aryl, heterocyclyl, OR<sub>3</sub>, or N(R<sub>3</sub>)<sub>2</sub>;R<sub>3</sub> is H, alkyl, aryl, or heterocyclyl;R<sub>4</sub> is H, CN, halogen, CF<sub>3</sub>, CO<sub>2</sub>R<sub>3</sub>, or C(O)N(R<sub>3</sub>)<sub>2</sub>;X is S, SO<sub>2</sub>, O, or NR<sub>3</sub>; andY is S, O, or NR<sub>3</sub>.

## INTERNATIONAL SEARCH REPORT

International Application No PCT/US2004/043950
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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D333/40 A61K31/381 A61P35/00 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 234 622 A (DUPHAR INTERNATIONAL RESEARCH B.V) 2 September 1987 (1987-09-02) claim 3; example VII -----	1,2
X	EP 1 176 139 A (SHIONOGI & CO., LTD) 30 January 2002 (2002-01-30) claim 1; compounds I36,I61 -----	1,2
X	US 2003/187002 A1 (MORTLOCK ANDREW ET AL) 2 October 2003 (2003-10-02) claims 1,3; table 23; compound 212 -----	1,2
X	US 2002/042428 A1 (MYERS JASON K ET AL) 11 April 2002 (2002-04-11) claim 1; examples 33,40 -----	1,2
	-/-	

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

4 May 2005

Date of mailing of the international search report

12/05/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Seelmann, I

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/043950

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99/55682 A (GEORGETOWN UNIVERSITY) 4 November 1999 (1999-11-04) page 1, line 5 - line 12; claim 1 -----	1-113
A	WO 03/006047 A (MERCK PATENT GMBH; CARR, FRANCIS, J; CARTER, GRAHAM; HELLENDORF, KOEN) 23 January 2003 (2003-01-23) page 6, line 13 - page 8, line 9 -----	1-113

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US2004/043950

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
EP 0234622	A	02-09-1987		AT 54143 T AU 594119 B2 AU 6885687 A BG 49383 A3 BR 8700705 A CN 87101917 A ,B CS 8701037 A2 DD 265315 A5 DE 3763409 D1 DK 76587 A EP 0234622 A1 HU 45483 A2 JP 62192353 A NZ 219285 A PL 264141 A1 SU 1496633 A3 US 4994485 A ZA 8701109 A		15-07-1990 01-03-1990 20-08-1987 15-10-1991 15-12-1987 06-01-1988 12-09-1989 01-03-1989 02-08-1990 20-08-1987 02-09-1987 28-07-1988 22-08-1987 26-04-1989 21-07-1988 23-07-1989 19-02-1991 28-10-1987
EP 1176139	A	30-01-2002		AU 2825000 A EP 1176139 A1 WO 0053573 A1		28-09-2000 30-01-2002 14-09-2000
US 2003187002	A1	02-10-2003		AU 6650501 A BG 107376 A BR 0111754 A CA 2412592 A1 CN 1496364 A CZ 20024120 A3 EE 200200715 A EP 1299381 A1 HU 0301236 A2 JP 2004501914 T NO 20026010 A NZ 522696 A PL 360439 A1 WO 0200649 A1 SK 18102002 A3 ZA 200209412 A		08-01-2002 30-09-2003 29-04-2003 03-01-2002 12-05-2004 12-03-2003 16-08-2004 09-04-2003 28-10-2003 22-01-2004 13-12-2002 27-08-2004 06-09-2004 03-01-2002 01-07-2003 19-02-2004
US 2002042428	A1	11-04-2002		AU 8287501 A AU 8291001 A AU 8464601 A EP 1311505 A2 JP 2004506734 T WO 0217358 A2 WO 0215662 A2 WO 0216355 A2 US 2002091135 A1 US 2002042429 A1 AU 8287301 A AU 8287401 A AU 8464501 A EP 1381603 A2 JP 2004506735 T WO 0216356 A2 WO 0216357 A2 WO 0216358 A2		04-03-2002 04-03-2002 04-03-2002 21-05-2003 04-03-2004 28-02-2002 28-02-2002 28-02-2002 11-07-2002 11-04-2002 04-03-2002 04-03-2002 04-03-2002 21-01-2004 04-03-2004 28-02-2002 28-02-2002 28-02-2002

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/043950

Patent document cited in search report	Publication date		Patent family member(s)		Publication date
US 2002042428	A1		US 2002052389 A1		02-05-2002
			US 2002040035 A1		04-04-2002
			US 2002049225 A1		25-04-2002
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WO 9955682	A	04-11-1999	AU 3669199 A		16-11-1999
			CA 2330458 A1		04-11-1999
			EP 1082310 A1		14-03-2001
			JP 2002513008 T		08-05-2002
			WO 9955682 A1		04-11-1999
			US 2002042423 A1		11-04-2002
-----					
WO 03006047	A	23-01-2003	BR 0211091 A		15-06-2004
			CA 2453406 A1		23-01-2003
			CN 1523996 A		25-08-2004
			WO 03006047 A2		23-01-2003
			EP 1409003 A2		21-04-2004
			HU 0400340 A2		30-08-2004
			JP 2004533845 T		11-11-2004
			MX PA04000339 A		04-05-2004
			US 2004185038 A1		23-09-2004
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

**PCT**

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

### FOR FURTHER ACTION See paragraph 2 below

International application No.  
PCT/US2004/043950

International filing date (day/month/year)  
29.12.2004

Priority date (day/month/year)  
30.12.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D333/40, A61K31/381, A61P35/00, G01N33/68

Applicant  
THE BRIGHAM AND WOMEN'S HOSPITAL, INC.

#### 1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

#### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

#### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Authorized Officer

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Telephone No. +49 89 2399-7480



10/585216

International application No.  
PCT/US2004/043950

AP20 Rec'd PCT/PTO 30 JUN 2006

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

**Box No. 1 Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
 a sequence listing  
 table(s) related to the sequence listing
  - b. format of material:  
 in written format  
 in computer readable form
  - c. time of filing/furnishing:  
 contained in the international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.
3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/043950

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,  
 claims Nos. 1, 2, 24-100 (industrial applicability), 101-106, 110-113

because:

the said international application, or the said claims Nos. 24-100 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. 1, 2 are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the whole application or for said claims Nos. 1, 2, 101-106, 110-113

the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard
the computer readable form	<input type="checkbox"/> has not been furnished
	<input type="checkbox"/> does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2004/043950

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**Box No. IV Lack of unity of invention**

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1.  In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
  - paid additional fees.
  - paid additional fees under protest.
  - not paid additional fees.
2.  This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
  - complied with
  - not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
  - all parts.
  - the parts relating to claims Nos.

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes:	Claims	3, 5-113
	No:	Claims	1, 2, 4
Inventive step (IS)	Yes:	Claims	3, 5-113
	No:	Claims	1, 2, 4
Industrial applicability (IA)	Yes:	Claims	1-23, 101-113
	No:	Claims	

2. Citations and explanations

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

PCT/US2004/043950

**Re Item III**

Claims 24-100 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

The initial phase of the search for claims 1 and 2 revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search and the examination have been restricted to the compounds of present claim 3 and 4. The subject-matter of claims 101-106 and 110-113 has only been searched in view of the scope of the compound claims.

**Re Item IV****Lack of unity of invention**

Claims 101-106 and 110-113 are not limited to the scope of the claimed compounds. The claimed activity as such is, however, already known in the art, a single general inventive concept between the claimed compounds and the assay and the kit for the use in relation with other compounds than those of the present application is not detectable. This single inventive concept is defined as "involving one or more of the same or corresponding special technical features", which serve to distinguish the current application from the prior art (establishes novelty) and are responsible for the inventive activity. An objection concerning the unity of the invention must be expected in the regional phase.

**Re Item V****1. PRIOR ART**

Reference is made to the following documents:

D1: EP-A-0 234 622

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/043950

D2: EP-A-1 176 139  
D3: US 2003/187002 A1  
D4: US 2002/042428 A1  
D5: WO 99/55682 A  
D6: WO 03/006047 A

**2. NOVELTY**

The subject-matter of claims 3, 5-113 is considered to be novel (Article 33(2) PCT). The essential structural difference between the claimed compounds and those of D1-D4 resides i.a. in the R2 substituent.

The subject-matter of claims 1 and 2 is at least anticipated by D1-D4 (Article 33(2) PCT), these documents represent only an arbitrary selection of the relevant prior art. D1-D4 disclose generic formula with overlapping definitions and examples falling within this overlap (cf. search report). According to page 58 (line 1-2) the compound of claim 4 was commercially available at the time of drawing up this application, therefore, novelty for this compound cannot be acknowledged.

**3. INVENTIVE STEP**

The subject-matter of claims 3-100 and 107-109 can be considered as involving an inventive step (Article 33(3) PCT). The document D5 is regarded as being the closest prior art to the subject-matter of these claims. It discloses HLA agonists and antagonists. The structures of the active compounds are, however, completely different from the presently claimed. The problem to be solved by the present invention is seen in the provision of further compounds with HLA activity. In view of the experimental part and the other information as given in the description, it can be assumed that this problem has been solved by the compound F15 (claim 4). The prior art D6 discloses further information which relates HLA-DM to HLA-DR. Due to the structural differences even the combined teaching of D5 and D6 would not motivate a man skilled in the art to arrive at the present invention.